PCT/US2004/029148

WO 2005/047813

-1-

# METHOD AND APPARATUS FOR PERFORMING OPTICAL IMAGING USING FREQUENCY-DOMAIN INTERFEROMETRY

## CROSS REFERENCE TO RELATED APPLICATION(S)

This application claims priority from U.S. provisional application no. 60/514,769 filed on October 23, 2003, the entire disclosure of which is incorporated herein by reference.

#### FIELD OF THE INVENTION

The present invention relates generally optical imaging, and more particularly to method and apparatus for performing optical imaging using frequency-domain interferometry.

## **BACKGROUND OF THE INVENTION**

As is known in the art, optical interferometric reflectometry is a powerful tool for performing non-invasive, high-resolution (~10 µm), cross-sectional imaging of a biological or other sample, to visualize micro-structural optical properties such as reflection, absorption, scattering, attenuation, birefringence, and spectroscopic analysis. There are a number of interferometric imaging techniques that are known in the art. These techniques in general can be divided into two major categories: (i) time-domain technique, and (ii) frequency-domain technique.

20

25

15

10

Low coherence interferometry ("LCI") is one of the tirne-domain techniques. This technique uses a scanning system to vary the reference arm length and acquire the interference signal at a detector. Then, the fringe pattern is demodulated to obtain the coherence envelope of the source cross correlation function. Optical coherence tomography ("OCT") is a technique for obtaining two- or three-dimensional images using LCI. OCT is described in U.S. Pat. No. 5,321,501 issued to Swanson et al. Multiple variants of the OCT techniques have been described, but many suffer from less than optimal signal to noise ratio ("SNR"), resulting in non-optimal resolution, low imaging frame rates, and poor depth of penetration. Power usage is a factor in such imaging techniques. For

10

15

20

25

30

WO 2005/047813 PCT/US2004/029148 -2-

example in ophthalmic uses, only a certain number of milliwatts of power are tolerable before thermal damage can occur. Thus, boosting power is not feasible to increase SNR in such environments. Nevertheless, it would be desirable to have an imaging method with superior SNR without appreciably increasing power requirements.

Insufficient SNR can also prevent the OCT technique from being used at a high frame rate which is important to avoid motion artifacts and overcome the short measurement time window available, for example, for in-vivo vascular imaging. Therefore, a way to improve SNR and imaging speed (e.g., the frame rate) is desired.

Spectral interferometry, or spectral radar, is one of the frequencydomain imaging techniques. In spectral radar, the real part of the cross spectral density of sample and reference arm light is measured with a spectrometer. Depth profile information can be encoded on the cross-spectral density modulation.

The use of spectral radar concepts to increase SNR of LCI and OCT has been described previously. This technique uses a charge coupled device ("CCD") with a large number of pixels (an order of 1,000) to reach scan ranges on the order of a millimeter. The fast readout of the CCD device makes high-speed imaging possible.

There are, however, a number of disadvantages associated with using a CCD device. First, CCD devices are relatively expensive compared to a singleelement photo-receiver. Secondly, the previously described method uses a single CCD to acquire the data. Since the charge storage capacity is limited, it requires a reduction of the reference arm power to approximately the same level as the sample arm power, giving rise to auto correlation noise on the sample arm light. In addition, since no carrier is generated, the 1/f noise will dominate the noise in this system. Thirdly, even with the short integration times of state of the art CCD technology, phase instabilities in the interferometer reduce fringe visibility of the cross spectral density modulation. This shortcoming makes the technique vulnerable to motion artifacts.

Coherent frequency-modulated continuous-wave reflectometry (C-FMCW) is another frequency domain technique known in the art. U.S. Patent Nos. 5,956,355 and 6,160,826 issued to Swanson et al. describes an optical imaging

WO 2005/047813 PCT/US2004/029148 -3-

method and apparatus using this technique. The previously described imaging method is based on using a continuously-tuned single-frequency laser as an optical source. The tuning wavelength range is required to be several tens of nanometers to achieve ranging resolution of less than 100 microns. The instantaneous linewidth of the laser must be less than approximately 0.1 nm to achieve a detection range on the order of 1.0 mm. The tuning rate should be greater than 10 kHz for high speed (e.g., video-rate) imaging. Although an external-cavity semiconductor laser can be configured to achieve mode-hop-free single-frequency tuning over several tens of nanometer, the tuning rate has been less than 1 Hz due to stringent requirement on mechanical stability. A way to overcome this speed difficulty is preferable.

5

10

15

20

25

30

It would, therefore, be desirable to provide a system and method to overcome the source availability and scan speed shortcomings of conventional LCI and OCT.

#### SUMMARY OF THE INVENTION

In accordance with exemplary embodiments of the present invention, an exemplary optical frequency domain imaging ("OFDI") system can include a multiple-frequency-mode (or multiple longitudinal or axial-mode) wavelength-swept laser source optically coupled to an interferometer containing a sample under study. The system can further include an arrangement which is configured to produce interferometric signals in quadrature between light reflected from a sample and a reference light and a detector disposed to receive the interferometric signals.

With such exemplary particular arrangement, an OFDI system which can operate with source powers that are relatively low compared with source powers of conventional systems and/or which operate at acquisition rates which are relatively high compared with acquisition rates of conventional systems may be provided. The use of a swept source results in an imaging system having reduced shot noise and other forms of noise which allows for much lower source powers, or much higher acquisition rates than conventional systems. This can lead to an increased detection sensitivity which results in the ability to provide

WO 2005/047813 PCT/US2004/029148
-4-

real time imaging. Such imaging speed can assist practitioners in gastrointestinal, ophthalmic and arterial imaging fields, where motion artifacts are a continuing problem. By increasing a frame rate while maintaining or improving the signal to noise ratio such artifacts can be minimized or in some cases eliminated. Exemplary embodiments of the present invention may also enable the screening of large areas of tissues with OFDI and allows enables the use of clinically viable screening protocols.

5

10

15

20

25

30

In one exemplary embodiment of the present invention, the wavelength-swept laser can be provided that may use an optical band-pass scanning filter in the laser cavity to produce a rapidly-swept multiple-frequency-mode output. By using an optical band-pass scanning filter in the laser cavity, it is not necessary to tune the laser cavity length to provide synchronous tuning of the laser spectrum. In other words, it does not require tuning the longitudinal cavity mode of the laser at the same rate as the center wavelength of the laser.

In another exemplary embodiment of the present invention, the detector can be a dual-balanced receiver disposed to accept interferometric signals and to suppress the relative intensity noise in the interferometric signals.

The gain in signal-to-noise ratio ("SNR") according to an exemplary embodiment of the present invention is advantageous over time-domain approaches such as OCT via a performance of the signal processing in the Fourier-domain. The SNR enhancement is by a factor of N, the ratio of the depth range to the spatial resolution. The enhancement factor N can reach a few hundreds to several thousand. This increase in SNR enables the imaging by a factor of N times faster, or alternatively allows imaging at the same speed with a source that has N times lower power. As a result, the exemplary embodiment of the present invention overcomes two important shortcomings of conventional LCI and OCT, e.g., source availability and scan speed. The factor N may reach more than 1,000, and allows construction of OFDI systems that can be more than three orders of magnitude improved from OCT and LCI technology currently in practice.

The gain in SNR is achieved because, e.g., the shot noise has a white noise spectrum. The signal intensity present at the detector at frequency  $\omega$  (or wavelength  $\lambda$ ) contributes only to the signal at frequency  $\omega$ , but the shot noise is

generated at all frequencies. By narrowing the optical band width per detector, the shot noise contribution at each frequency can be reduced, while the signal component remains the same.

5

10

15

20

25

30

Exemplary embodiments according to the present invention improves current data acquisition speeds and availability of sources compared with OCT. Shot noise is due to the statistical fluctuations of the current that are due to the quantized or discrete electric charges. The reduction of shot noise allows for much lower source powers or much higher acquisition rates. Limitations in current data acquisition rates (~ 4 frames/sec) are imposed by available source power and availability of fast mechanisms for scanning delay. An increase in the sensitivity of the detection by a factor of 8 would allow real time imaging at a speed of about 30 frames per second. An increase of the sensitivity by a factor of about 1,000-2,000 allows for the use of sources with much lower powers and higher spectral bandwidths which are readily available, cheaper to produce, and can generate higher resolution OFDI images.

For ophthalmic applications of OFDI, efficient detection preferably allows for a significant increase of acquisition speed. One limitation in ophthalmic applications is the power that is allowed to enter the eye according to the ANSI standards (approximately 700 microwatts at 830 nm). Current data acquisition speed in ophthalmic applications is approximately 100-500 A-lines per second. The power efficient detection technique of the present invention would allow for A-line acquisition rates on the order of about 100,000 A-lines per second, or video rate imaging at about 3,000 A-lines per image.

To achieve at least some of the goals of the present invention, an apparatus and method according an exemplary embodiment of the present invention are provided. In particular, at least one first electro-magnetic radiation may be provided to a sample and at least one second electro-magnetic radiation can be provided to a non-reflective reference. A frequency of the first and/or second radiations varies over time. An interference is detected between at least one third radiation associated with the first radiation and at least one fourth radiation associated with the second radiation. Alternatively, the first electro-magnetic radiation and/or second electro-magnetic radiation have a spectrum which changes over time. The spectrum may contain multiple frequencies at a

WO 2005/047813 PCT/US2004/029148
-6-

particular time. In addition, it is possible to detect the interference signal between the third radiation and the fourth radiation in a first polarization state. Further, it may be preferable to detect a further interference signal between the third and fourth radiations in a second polarization state which is different from the first polarization state. The first and/or second electro-magnetic radiations may have a spectrum whose mean frequency changes substantially continuously over time at a tuning speed that is greater than 100 Tera Hertz per millisecond.

5

10

15

20

25

30

In one exemplary embodiment of the present invention, the third radiation may be a radiation returned from the sample, and the at least one fourth radiation is a radiation returned from the reference. The frequency of the first, second, third and/or fourth radiation may be shifted. An image can be generated based on the detected interference. A probe may be used which scans a transverse location of the sample to generate scanning data, and provides the scanning data to the third arrangement so as to generate the image. The scanning data may include the detected interference obtained at multiple transverse locations on the sample. At least one photodetector and at least one electrical filter may be used which follow a photodetector, which is followed by an electrical filter. The electric filter ma be a bandpass filter having a center frequency that is approximately the same as a magnitude of the frequency shift by the frequency shifting arrangement. A transmission profile of the electrical filter can vary substantially over its passband. The probe may include a rotary junction and a fiber-optic catheter. The catheter can be rotated at a speed higher than 30 revolutions per second. At least one polarization modulator may be provided.

At least one polarization diverse receive and/or a polarization diverse and dual balanced receiver may be used. It is further possible to track the phase difference between:

- the first electromagnetic radiation and the second electromagnetic radiation, and/or
- the third electromagnetic radiation and the fourth electromagnetic radiation.

According to still another exemplary embodiment of the present invention, the first and second electro-magnetic radiations can be emitted, at least one of which has a spectrum whose mean frequency changes substantially

-7-

5

10

15

20

25

30

continuously over time at a tuning speed that is greater than 100 Tera Hertz per millisecond.

According to still a further exemplary embodiment of the present invention, an apparatus is provided. Such apparatus includes at least one first arrangement providing at least one first electro-magnetic radiation to a sample and at least one second electro-magnetic radiation to a reference. The apparatus also includes t least one second arrangement adapted for shifting the frequency of the first electro-magnetic radiation and the second electromagnetic radiation, and an interferometer interfering the first and second electro-magnetic radiations to produce an interference signal. Further, the apparatus includes at least one second arrangement detecting the interference between the first and second electro-magnetic radiations.

Further, according to another exemplary embodiment of the present invention, a system, method, software arrangement and storage medium are provided for determining particular data associated with at least one of a structure and composition of a tissue. In particular, information associated with an interferometric signal is received which is formed from at least one first electromagnetic radiation obtained from a sample and at least one second electromagnetic radiation obtained from a reference. The first and/or second electromagnetic radiations is/are frequency-shifted. The information is sampled to generate sampled data in a first format. Further, the sampled data is transformed into the particular data that is in a second format, the first and second format being different from one another.

#### BRIEF DESCRIPTION OF THE DRAWINGS

For a more complete understanding of the present invention and its advantages, reference is now made to the following description, taken in conjunction with the accompanying drawings, in which:

FIG. 1 is a block diagram of a time-domain optical coherence tomography ("OCT") system;

PCT/US2004/029148

- FIG. 2 is a block diagram of a system which performs frequency-domain imaging using a spectral radar technique;
- FIG. 3A is a block diagram of a system which performs frequencydomain imaging using a coherent single-frequency tuning source according to one exemplary embodiment of the present invention;
- FIGS. 3B and 3C are graphs of wavelength versus amplitude which taken together illustrate the occurrence of a frequency shift generated by the system of Fig. 3A;
  - FIG. 3D is a graph of a beat signal generated by the system of FIG.
- 10 3A;

5

15

20

25

30

- FIG. 4A is a block diagram of a system which performs frequencydomain imaging using a multiple-longitudinal-mode wavelength-swept source according to another exemplary embodiment of the present invention;
- FIGS. 4B and 4C are graphs of a wavelength spectrum which taken together illustrate the occurrence of a shift in the spectrum generated by the system of Fig. 4A;
- FIG. 4D is a graph of a beat signal generated by the system of FIG. 4A;
- FIG. 5 is a block diagram of a system which performs frequencydomain imaging using a wavelength-swept source according to another exemplary embodiment of the present invention;
- FIG. 6 is a block diagram of an optical wavelength tunable filter arrangement according to an exemplary embodiment of the present invention;
- FIG. 7 is a block diagram of a wavelength-swept laser arrangement according to an exemplary embodiment of the present invention;
- FIG. 8A is an exemplary graph of a laser output spectrum as measured at an output of the wavelength-swept laser arrangement of FIG. 7;
- FIG. 8B is an exemplary graph of a laser output as measured at an output of the wavelength-swept laser of FIG. 7;
- FIG. 9A is a block diagram of a wavelength tunable filter arrangement bearing a polygonal mirror according to yet another exemplary embodiment of the present invention;

10

15

20

25

30

- FIG. 9B is a block diagram of a wavelength tunable filter arrangement having reflective disk according to still another exemplary embodiment of the present invention;
- FIG. 10A is a block diagram of an optical frequency domain imaging ("OFDI") system which includes a wavelength-swept laser and a polarization diversity-balanced detection ("PDBD") circuit according to a further exemplary embodiment of the present invention;
- FIG. 10B is a block diagram of an exemplary probe arrangement shown in FIG. 10A;
- FIG. 10C is a plurality of graphs illustrating exemplary outputs of a carrier-frequency heterodyne detection using the system of FIG. 10A;
- FIG. 11 is an exemplary in-vivo image of a human finger tip obtained using exemplary embodiments of the present invention;
- FIG. 12 is a block diagram of a phase tracker arrangement according to an exemplary embodiment of the present invention;
- FIG. 13 is a block diagram of an exemplary embodiment of the OFDI system according to the present invention having the phase tracker;
- FIGS. 14A-14C are flow diagrams which illustrate an exemplary technique for a phase tracker operation according to the present invention;
- FIG. 15 is a simplified diagram of the OFDI system according to another exemplary embodiment of the present invention;
- FIGS. 16(a) and 16(b) are graphs of effects of a frequency shift according to the present invention, i.e., depth versus signal frequency;
- FIG. 17 is a block diagram of the OFDI system employing two acousto-optic frequency shifters according to still another exemplary embodiment of the present invention;
- FIGS. 18(a) and 18(c) are graphs of point spread functions measured without a mapping process according to the present invention; and
- FIGS. 18(b) and 18(d) are graphs of point spread functions measured with the mapping process according to the present invention.
- Throughout the drawings, the same reference numerals and characters, unless otherwise stated, are used to denote like features, elements, components, or portions of the illustrated embodiments. Moreover, while the present invention

will now be described in detail with reference to the Figures, it is done so in connection with the illustrative embodiments.

#### DETAILED DESCRIPTION

FIG. 1 shows an exemplary prior art time domain optical coherence tomography ("OCT") system 10 which includes a broadband source 12 that provides a signal to a first arm 14a of two-by-two splitter 14. The splitter divides the signal provided thereto at port 14a, and provides a first portion of the signal at a port 14b coupled to a reference arm 16. The splitter 14 also provides a second portion of the signal at a port 14c coupled to a sample arm 18.

10

5

The sample arm 18 terminates at a sample volume 19 and an arrangement 22 for providing a lateral scan of the sample volume is disposed in the sample arm 18 prior to the sample volume 19. The reference arm 16 terminates in an arrangement 20 for providing an axial scan. The arrangements 20 and 22 operate as is generally known in the art.

15

Signals reflected from the means 20 and sample volume 19 back along the reference and sample arms 16, 18 respectively, are coupled back into respective ports 14b, 14c of the splitter 14 and are coupled to a detector 24 which produces axial scan data 26 as is generally known. U.S. Patent 6,341,036, the entire disclosure of which is incorporated herein by reference, describes systems similar to the one described above and shown in FIG. 1.

20

In general, on scanning the reference arm path length 16, interference fringes are formed corresponding to positions that match the distance to the three structures 19a, 19b, 19c in the sample volume 19. The single detector 24 is used to detect the interference fringes. By envelope detection of the fringe patterns, an image 26 is constructed that maps tissue reflectivity to a given location.

25

30

As will be apparent from certain exemplary embodiments described herein below, an exemplary embodiment of the present invention relates to a system which utilizes a detection principle based upon Spectral Radar concepts (further referred to as Spectral Domain OCT) and/or a hybrid method between Spectral Domain and Time Domain OCT that is preferably more sensitive than

10

15

current state of the art Time Domain OCT, allowing a substantial increase in the acquisition speed to resolution ratio.

Analysis of the Signal to Noise Ratio ("SNR") in Time Domain OCT has been previously described in related publications. The interference fringe peak amplitude in time domain OCT is given by

$$I_{peak} = \sqrt{P_{ref} \ p_{sample}} \ , \tag{1}$$

with  $P_{ref}$ ,  $P_{sample}$  the reference and sample arm power in Watts, respectively. In terms of electrical power at the detector, the signal in units  $[A^2]$  is defined as

$$S = \eta^2 e^2 P_{ref} P_{sample} / E_v^2, \qquad (2)$$

with  $\eta$  the quantum efficiency, e the charge quantum and  $E_{\nu} = hc/\lambda$  the photon energy. The reference and sample arm powers are given by the respective reflected spectral densities,

$$P_{ref,sample} = \int S_{ref,sample}(\omega) d\omega.$$
 (3)

Assuming that the reference and sample spectral densities are equal to the source spectral density  $S(\omega)$ , where the sample arm spectral density is attenuated by a large factor, i.e.,  $S_{ref}(\omega) = S(\omega)$ ,  $S_{sample}(\omega) = \alpha S(\omega)$  with  $\alpha \langle \langle 1 \rangle$ , and inserting the above expression of reference and sample arm into the original definition of the signal gives,

$$S = \eta^2 e^2 \alpha \left| \int S(\omega) d\omega \right|^2 / E_v^2. \tag{4}$$

Three contributions to the total noise of OCT signals are: (i) thermal noise, (ii) shot noise and (iii) relative intensity noise. Thermal noise is generated by the feedback resistor, shot noise is related to the finite nature of the charge quantum resulting in statistical fluctuations on the current, and relative intensity noise is related to the temporal fluctuations due to chaotic character of classical light sources. These three contributions to the noise density in units [A²/Hz] are given by,

$$N_{noise}(f) = \frac{4kT}{R_{fb}} + \frac{2\eta e^2 P_{ref}}{E_{v}} + 2\left(\frac{\eta e P_{ref}}{E_{v}}\right)^2 \tau_{coh} , \qquad (5)$$

k is Boltzmann's constant, T the temperature in Kelvin,  $R_{fb}$  the value of the feedback resistor, and  $\tau_{coh}$  the coherence time of the source. Coherence time is

15

20

25

30

related to the full spectral width at half maximum  $\Delta\lambda$  of a Gaussian source by the following relation,  $\tau_{coh} = \sqrt{2 \ln 2/\pi} \, \lambda_0^2/(c\Delta\lambda)$ . Shot noise limited detection is achieved when the second term in Eq. (5) dominates the other noise contributions.

The signal to noise ratio (SNR) is given by

$$SNR = \frac{S}{N_{noise}(f)BW}, (6)$$

with BW the signal bandwidth, and parameters S and  $N_{\text{noise}}(f)$  as described above.

# Spectral Domain OCT using a Spectrometer and CCD array detector

The best signal to noise performance of Time Domain OCT systems is obtained when the noise is shot noise limited. Shot noise can be reduced significantly by replacing the single element detector with a multi-element array detector. When the detection arm light is spectrally dispersed on the array detector, each element of the array detects a small wavelength fraction of the spectral width of the source. The shot noise is preferably reduced by a factor equal to the number of elements of the array. The principle of the signal to noise improvement is based on the white noise characteristic of shot noise and the observation that only electromagnetic waves of the same wavelength produce interference fringes.

The shot noise power density  $N_{noise}$  (f) (in units [W/Hz],  $[A^2/Hz]$  or  $[V^2/Hz]$ ) is proportional to the current (or equivalently the optical power times the quantum efficiency) generated in the detector. For a monochromatic beam of wavelength  $\lambda_I$  entering the interferometer, the fringe frequency or carrier f at the detector is determined by the velocity v of the mirror,  $f_1 = 2v/\lambda_1$ . The shot noise is proportional to the power (or spectral density  $S(\omega)$ ) at wavelength  $\lambda_I$ . A second wavelength  $\lambda_2$  is preferably coupled into the interferometer. A second fringe frequency or carrier at frequency  $f_2 = 2v/\lambda_2$  is simultaneously present. The shot noise at this second frequency is preferably the sum of the shot noise generated by the optical power at wavelength  $\lambda_I$  and  $\lambda_2$ . Also, at frequency  $f_I$  the shot noise is the sum of the shot noise generated by the optical power at wavelength  $\lambda_I$  and  $\lambda_2$ . Thus, at both frequencies a cross-shot noise term is generated by the simultaneous presence of both wavelengths at the detector. By spectrally dispersing each

10

20

25

30

wavelength to a separate detector, the cross shot noise term can be eliminated. In this way, Spectral Domain OCT offers a significant improvement of signal to noise ratio over Time Domain OCT systems.

The OCT signal is most easily described in the space domain. For a single object in the sample arm, the interference term of the OCT signal is proportional to the real part of the Fourier transform of the source spectrum  $S(\omega)$ ,

$$I(\Delta z)oc \operatorname{Re} \left(\exp(ik\Delta z)S(k)dk\right),$$
 (7)

with  $\Delta z$  the path length difference between sample and reference arm and k the wave vector. As a function of time, the OCT signal is given by,

$$I(t)oc \operatorname{Re} \left[ \exp(2i\omega rv/c)S(\omega)d\omega \right],$$
 (8)

with  $\nu$  the reference arm mirror velocity. The frequency spectrum of the signal is given by a Fourier transform of the signal in the time domain, resulting in a complex function. The absolute value of this function is equal to the spectral density.

15 
$$|I(f)| = \left| \int I(t)e^{2i\pi ft} dt \right| = S(\pi f c/\nu),$$
 (9)

which shows that the signal bandwidth is directly proportional to the source spectral width and scales linearly with the reference arm mirror velocity, i.e., imaging speed. Eq. (9) also preferably directly relates the absolute value of the frequency spectrum, |I(f)| to the signal S (see Eq. (4)). Eq. (9) also demonstrates that each angular frequency of the light source or equivalently each wavelength of the source is represented at its own frequency in the measured interferometric signal. The depth profile information I(t) can be obtained from the complex cross spectral density, |I(f)| by a Fourier transform.

The complex cross spectral density can also be obtained by splitting the signal I(t) in several spectral bands using a dispersive or interferometric element. At each detector, only part of the complex cross spectral density is determined. Combining the cross spectral densities of each detector, the full spectral density of the signal are retrieved. Thus, the same information can be obtained by separating spectral components to individual detectors. Combining the signal of all detectors in software or hardware would result in the same signal as obtained with a single detector.

25

In the detection arm, the spectrum can be split into two equal halves, where two detectors each detect one half of the spectrum. According to Eq. (9), the frequency spectra at detectors 1 and 2 are given by

$$|I_1(f)| = S(\pi f c/\nu)$$
 for  $f < f_0, I_1(f) = 0$  for  $f > f_0$  and

 $I_2(f) = 0$  for  $f < f_0$ ,  $|I_2(f)| = S(\pi f c/\nu)$  for  $f > f_0$ , respectively. The frequency spectrum as would be acquired by a single detector in time domain OCT is given by the sum of  $I_1(f)$  and  $I_2(f)$ ;  $I(f) = I_1(f) + I_2(f)$ . Thus, the signal S after combining the spectra is equal, however  $I_1(f) = 0$  for  $f > f_0$  and  $I_2(f) = 0$  for  $f < f_0$ , the bandwidth BW per detector can be reduced by a factor of 2.

The noise is determined by the sum of the shot noise contributions at detectors one and two. From Eqs. (5) and (6), the shot noise per detector is proportional to the reference arm power at the detector times the bandwidth for the detector. Since the spectrum was split in equal halves, the reference power at detectors 1 and 2 is, respectively,

$$P_{ref}^1 = 0.5 P_{ref}, \quad P_{ref}^2 = 0.5 P_{ref}.$$
 (10)

The sum of the shot noise contribution for the two detectors is,

$$N_{noise}^{SD} oc P_{ref}^1 \times 0.5BW + P_{ref}^2 \times 0.5BW = 0.5P_{ref}BW$$
, (11)

which may compared with the shot noise of a single detector in time domain OCT,

$$N_{noise}^{TD} \propto P_{ref}BW. \tag{12}$$

Thus, by spectrally dispersing the detection and light over two separate detectors, the signal remains the same, while the noise is reduced by a factor of 2, resulting in a net SNR gain by a factor of 2.

Extending the above analysis, it can be demonstrated that the shot noise contribution is reduced by a factor equal to the number of detectors. The sum of shot noises for N detector elements, where each detector element receives one Nth of the total reference power, is given

$$N_{noise} = \frac{2\eta e^2 P_{ref}}{E} \frac{BW}{N} \ . \tag{13}$$

20

25

The signal is the same as in Time Domain OCT, and the SNR ratio for Spectral Domain OCT is given by,

$$\frac{S}{N_{\text{police}}} = \frac{\eta P_{\text{sample}} N}{2E_{\text{u}} BW} \,. \tag{14}$$

Thus Spectral Domain OCT enables a SNR improvement over Time Domain OCT of a hundred to a thousand fold, depending on the number of detector elements N. Using a charge coupled array or an integrating device as a detector, such as, but not limited to, a line scan camera, the ratio N/BCW is replaced by the integration time  $\tau_i$  of the array, which results in,

$$\frac{S}{N_{noise}} = \frac{\eta P_{sample} \, \tau_i}{2E_{\nu}} \,. \tag{15}$$

FIG. 2 shows an exemplary Spectral Domain OCT system 100 which includes an interferometer 102 with a source arm 104, a sample arm 106, a reference arm 108, and a detection arm 110 with a spectral separating unit 112, a detector array 114 comprised of a plurality of detectors and a like plurality of amplifiers 116. The amplifiers 116 are coupled through optional analog processing electronics (not shown, but known to those having ordinary skill in the art), and A/D converters (not shown, but known to those skilled in the art) for conversion of signals and through digital band pass filtering ("BPF") units 122 to a processing and display unit 124.

The processing and display unit 124 executes data processing and display techniques, and can optionally include the digital band pass filtering ("BPF") units 122 as well as Digital Fast Fourier Transforms (""DFFTs") circuits (not shown), in order to provide coherent combination of signals and to perform the data processing and display functions. The detector array 114 may be 1 x N for simple intensity ranging and imaging and/or Doppler sensitive detection, 2 x N for dual balanced detection, 2 x N for simple intensity ranging and/or polarization and/or Doppler sensitive detection, or 4 x N for combined dual balanced and polarization and/or Doppler sensitive detection. Alternatively, an M x N array may be used for arbitrary number "M" of detectors 114 to allow detection of transverse spatial information on the sample 130.

WO 2005/047813 PCT/US2004/029148 -16-

Electro-magnetic radiation (e.g., light) is transmitted from the source along the source arm 104 to the splitting unit via and is split between the reference arm 108 and the sample arm 106. The light propagates along the sample arm to the tissue sample 130 and through the reference arm 108 to a wavelength dependent phase arrangement. The light is reflected from the sample and the wavelength dependent phase arrangement back toward the splitting unit where at least portions of the reflected light are directed toward the spectral separating unit 112 (which may be provided as a grating for example). The detection arm light is dispersed by the spectral separating unit 112 and the spectrum is imaged onto the detector array 114. By stepping the reference arm 108 length over a distance  $\lambda/8$ , the cross spectral density of reference arm 108 and sample arm 106 light can be determined. The processing and display unit received the signals fed thereto and performs a Fourier transform of the cross spectral density to generate depth profile information.

15

20

10

5

FIG. 3A shows a block diagram of an exemplary system according to the present invention which illustrates basic principles of a coherent frequency modulated continuous Wave ("C-FMCW") system using a single-frequency tuning source. A monochromatic laser light 70 operable as a frequency chirped laser provides a light signal to an input 72a of a coupler 72. The coupler 72 divides the light signal into a reference arm 80 which terminates in a reference mirror 82 and a sample arm 84 which terminates in a sample 86. The light propagates down paths 80, 84 and reflects from the reference mirror 82 and sample mirror 86 to provide, via coupler 72, interference signals which are detected by a photo-detector 88.

25

30

As shown in graphs of FIGS. 3B-3D, when there is an optical delay between two reflected light signals 90 (FIG. 3B) and 92 (FIG. 3C), respectively, a beat signal 94 (see FIG. 3D) having a frequency f may be detected at the photo detector 88. Where there are multiple reflection points in the sample along the axis, the interference consists of beat notes having frequencies which are proportional to the optical delay difference between the reflection (scatter) point in the sample and the reference mirror. The power of each beat frequency component is proportional to the reflectivity of the scatter. Therefore, the image of the sample can be constructed by Fourier transform of the interference data.

Referring now to FIGS. 4A-4D, in which like elements described above and shown in FIGS 3A-3D are provided having the same reference designations, an optical frequency domain imaging ("OFDI") system according to an exemplary embodiment of the present invention includes a wavelength-swept laser source 95 (also referred to herein as a frequency swept source 95) which provides a laser output spectrum comprised of multiple longitudinal modes to an input of a coupler 72. The coupler 72 divides the signal fed thereto into the reference arm 80 which terminates in the reference mirror 82 and the sample arm 84 which terminates in the sample 86. The optical signals reflect from the reference mirror 82 and the sample 86 to provide, via coupler 72, a spectrum of signals which are detected by a photo-detector 88.

The center (or mean) wavelength of the signal spectrum is tuned in time by the creation of new longitudinal modes at the leading side of the spectrum and the annihilation of the modes at the trailing side of the spectrum.

15

20

25

10

5

The same principles described above with reference to FIGS. 3A-3D also apply to the OFDI technique using a wavelength-swept laser source 95. Similar to the case of a C-FMCW system (e.g., the system of FIG. 3A described above), a beat signal 94 can be produced. In the case of the OFDI system that uses a wavelength-swept laser source, the beat signal 94 can be generated having a beat frequency f which corresponds to the difference in the center frequency of the lights, 96 and 98, from the reference and sample, respectively.

The frequency spacing between longitudinal modes should be substantially larger than the detection bandwidth. The mode beat frequency (relative intensity noise peaks) can be removed by a proper electronic filter, such as low pass filter, prior to digitization. The interference signal 94 contains a frequency component that is proportional to the optical delay. Furthermore, the image of the sample can be constructed by Fourier transform of the digitized interference data.

30

In one exemplary embodiment of the present invention, the wavelength-swept laser 95 can be provided which utilizes an optical band-pass scanning filter in the laser cavity to produce a rapidly-swept multiple-frequency-mode output. Exemplary filters according to the present invention is described below in conjunction with FIGS. 6 and 9A. By using an optical band-pass

scanning filter in the laser cavity, it is not necessary to tune the laser cavity length to provide synchronous tuning of the laser spectrum. Indeed, such arrangement does not require tuning the longitudinal cavity mode of the laser at the same rate as the center wavelength of the laser.

Using the OFDI techniques, a single pixel of the image can be constructed from the signal that is recorded as a function of time over the duration of one A-scan through Fourier transform. This is different from the TD OCT where a single pixel is constructed from the data measured at a short period time within one A-scan. The detection bandwidth to acquire the same number of data within the same A-scan period is approximately the same for both TD and FD OCT. However, the Fourier transform used for the OFDI technique effectively improves the signal-to-noise ratio compared to TD OCT by constructing a single image pixel from many data points acquired over the whole A-scan period. This effect can result in an "effective" detection bandwidth that is N-times larger than the actual detection bandwidth. Therefore, the SNR may be improved by N times, where N is the number of (digitized) data points in the Fourier transform. It can be shown that SNR in a shot noise limited case is given by:

$$\frac{S}{N_{\text{noise}}} = \frac{\eta P_{\text{sample}} N}{2E_{y} BW} \tag{16}$$

20

25

30

5

10

15

Due to the narrowband output spectrum of the wavelength-swept source, however, the relative intensity noise (RIN) can be significantly higher than that of a CW broadband light source. For a thermal light, RIN is given by  $1/\Delta \nu$  where  $\Delta \nu = c \cdot \Delta \lambda / \lambda^2$  is the optical bandwidth of the (instantaneous) source output. For a laser light, RIN results from different statistics and therefore has a different value than the thermal light. For FD-OCT, a wavelength-swept laser with a low RIN level is preferred. The laser light with multiple longitudinal modes may have a similar RIN level as the thermal light with the same linewidth. In this case, a means to suppress the RIN is critical to have sufficient SNR, such as the dual balanced detection.

Use of a swept source results in a system having reduced shot noise and other forms of noise which allows for much lower source powers, or much higher acquisition rates than current systems. The increased detection sensitivity allows for real time imaging. Such imaging speed can assist with a problem of motion artifacts, such as in gastrointestinal, ophthalmic and arterial imaging environments. By increasing the frame rate while maintaining or improving the signal to noise ratio such artifacts can be minimized. The present invention also enables one to screen large areas of tissues with the OFDI technique, and allows clinical yiable screening protocols using this method.

10

5

For ophthalmic applications of OFDI, the efficient detection preferably allows for a significant increase of acquisition speed. A possible limitation in ophthalmic applications is the power that is allowed to enter the eye according to the ANSI standards (approximately 700 microwatts at 830 nm). Current data acquisition speed in ophthalmic applications is approximately 100-500 A-lines per second. The power efficient detection would allow for A-line acquisition rates on the order of about 100,000 A-lines per second, or video rate imaging at about 3,000 A-lines per image.

20

15

The gain in SNR is achieved because the shot noise has a white noise spectrum. The signal intensity present at the detector at frequency  $\omega$  (or wavelength  $\lambda$ ) contributes only to the signal at frequency  $\omega$ , but the shot noise is generated at all frequencies. By narrowing the optical band width per detector, the shot noise contribution at each frequency can be reduced, while the signal component remains the same.

25

30

FIG. 5 shows an exemplary embodiment of a system 99 for performing optical imaging using frequency-domain interferometry ("OFDI") which includes a frequency swept source 100 that emits a narrowband spectrum of which the center wavelength is tuned continuously and repeatedly in time across the bandwidth of the gain medium in the source. The instantaneous emission spectrum consists of a plurality of frequency modes of the light source. The frequency swept source 100, may be provided in a variety of different ways, some of which are described below. The source 100 may, for example, be provided from various gain media, tunable wavelength filters, cavity configurations.

Devices and methods are known in the art to provide a rapidly-tuned wavelength-swept laser source, such as solid-state lasers, active-ion-doped waveguide lasers, and fiber lasers. A wavelength-swept laser in a mode-locked regime can also be used with potential advantage of a lower relative intensity noise (RIN) in a frequency region between harmonics of longitudinal-mode beat frequencies. An optical saturable absorber may be incorporated inside a laser cavity or after the output port of the source to lower RIN level.

5

10

15

20

25

30

The light provided from swept source 100 is directed toward a fiberoptic coupler 102 which divides the light fed thereto into a reference arm 103 and
a sample arm 104. In this exemplary embodiment, the coupler 102 has a 90:10
power splitting ratio with 90% of the power being directed toward the sample arm.
Those of ordinary skill in the art would understand, however, that other coupling
ratios for the coupler 102 may also be used. The particular coupling ratio to use in
any particular application should be selected such that an amount of power is
provided to both the reference arm and the sample arm to allow for proper
operation of the exemplary system according to the present invention.

The power provided to the sample arm passes though a circulator 111, and illuminates a sample 136 to be imaged through a transverse-scanning imaging probe. The reference arm provides preferably a fixed optical delay. The lights reflected from a reference mirror 124 and from within the sample 136 can be directed through the respective circulators 110, 111 toward a fiber-optic beam splitter (or fused coupler) 150 and interfere between each other to produce interference signals.

It is desirable that the combining coupler 150 have an equal splitting ratio with minimal polarization dependence and wavelength dependence over the wavelength tuning range of the source. A deviation from equal splitting results in reduction of common mode rejection ratio ("CMRR") of the dual balanced detection. In one embodiment, the combining coupler 150 is preferably provided as a bulk broadband beam splitter. Those of ordinary skill in the art would understand that other types of couplers (including but not limited to wavelength-flattened fiber fused couplers) may also be used.

The interference signals are received by a dual balanced receiver 151.

Output of the receiver 151 is provided to a computing arrangement (e.g., a data

WO 2005/047813 PCT/US2004/029148 -21-

acquisition board and computer 160), such that the output is digitized and processed by the computer arrangement to produce an image. The data acquisition, transverse scanning, and wavelength tuning are synchronously controlled.

5

10

FIG. 6 shows an exemplary light source 100' which may, for example, be adapted for use as a frequency swept source (such as frequency swept source 100 described above with reference to FIG. 5) is provided from an optical filter 170, coupled through a lens 172 and a light path 174 to a light source/controller 176 (hereinafter referred to as "light controller 176"). The light controller 176 may, in turn, be coupled to one or more applications 178. The applications 178 may, for example, correspond to optical imaging processes and/or optical imaging systems, laser machining processes and systems, photolithography and photolithographic systems, laser topography systems, telecommunications processes and systems. Thus, the exemplary light source 100' provided from the filter 170 and the light controller 176 may be used in a wide variety of different applications, certain general examples of which are described herein.

15

20

25

As shall be described in further detail below, the filter 170 allows the light source 100' to operate as a frequency swept source which emits a spectrum of which the center wavelength can be tuned continuously and repeatedly in time across the bandwidth of the light controller 176. Thus, light source 100' may have an instantaneous emission spectrum comprised of a plurality of frequency modes of the light source/controller 176. In this exemplary embodiment, the optical wavelength filter 170 is configured as a reflection-type filter in that the input and output ports are identical. Thus, light path 174 may be provided, for example, as an input/output optical fiber and lens 172 may correspond to a collimating lens. Although the filter 170 in FIG. 6 is shown coupled to one or all of applications 178 through the light controller 176, it is possible to directly couple the filter 170 to one or more of the applications 178. Alternatively, it is possible to couple the filter 170 to one or more of the applications 178 through a device other than a light controller.

30

In the exemplary embodiment according to the present invention, the light controller 176 can include a number of systems that are specifically adapted to transmit a beam of light (in one embodiment, a collimated beam of light)

having a broad frequency (f) spectrum. In particular, the beam of light can include a plurality of wavelengths, within the visible light spectrum (e.g., red, blue, green). The beam of light provided by the light controller can also include a plurality of wavelengths that are defined outside of the visible spectrum (e.g., infrared).

5

10

15

20

25

30

As shall be described in greater detail below with reference to FIG. 7, in one exemplary embodiment of the present invention, the light controller 176 can include a unidirectional light transmission ring. In another exemplary embodiment to be described in detail in conjunction with FIG. 9 below, the light controller 176 can include a linear resonator system. The filter 170 includes a wavelength dispersing element 180 adapted to receive the beam of light from the light controller 176 and to separate the beam of light into a plurality of different wavelengths of light each directed along a light path as is known. The wavelength dispersing element 180 can include one or more elements adapted to receive the beam of light from the light controller 176, and to separate the beam of light into a plurality of wavelengths of light each directed along a light path. The wavelength dispersing element 180 is further operative to direct the plurality of wavelengths of light in a plurality of angular directions or displacements with respect to an optical axis 182. In one exemplary embodiment of the present invention, the wavelength dispersing element 180 can include a light dispersion element, such as a reflection grating 184. The wavelength dispersing element 180 could alternatively be provided as a transmission grating (e.g. a transmission type grating such as Dickson-type holographic grating), a prism, a diffraction grating, an acousto-optic diffraction cell or combinations of one or more of these elements.

wavelength towards a lens system 186 along paths which are at an angle with respect to the optical axis 182. Each angle is determined by the wavelength dispersing element 180. The lens system 186 can include one or more optical elements adapted to receive the separated wavelengths of light from the wavelength dispersing element 180 and to direct or steer and/or focus the wavelengths of light to a predetermined position located on a beam deflection

device 188. The beam deflection device 188 can be controlled to receive and selectively redirect one or more discrete wavelengths of light back along the

The wavelength dispersing element 180 directs light at each

optical axis 182 through the lens system 186 to the wavelength dispersing element 180 and back to the light controller 176. Thereafter, the light controller 176 can selectively direct the received discrete wavelengths of light to anyone or more of the applications 178. The beam deflecting device 188 can be formed and/or arranged in a number of ways. For example, the beam deflecting device 188 can be provided from elements including, but not limited to, a polygonal mirror, a planar minor disposed on a rotating shaft, a minor disposed on a galvanometer, or an acousto-optic modulator.

5

10

15

20

25

30

In the exemplary embodiment shown in FIG. 6, the dispersing element 186 includes a diffraction grating 184, a lens system 186 (which has first and second lenses 190, 192 to form a telescope 193), and the beam deflecting device 188 which is shown as a polygon mirror scanner 194. The telescope 193 is provided from the first and second lenses 190, 192 with 4-f configuration. The first and second lenses 190, 192 of the telescope 193 are each substantially centered on the optical axis 182. The first lens 190 is located at a first distance from the wavelength dispensing element 180 (e.g., diffraction grating 184), which is approximately equal to the focal length F1 of the first lens 190. The second lens 192 is located a second distance from the first lens 190, which is approximately equal to the sum of the focal length F1 of the first lens 190 and the focal length F2 of the second lens 192. In this exemplary arrangement, the first lens 190 can receive the collimated discrete wavelengths of light from the wavelength dispersing element 180, and may effectively perform a Fourier Transform on each one of the collimated one or more discrete wavelengths of light to provide an equal one or more converging beams projected onto an image plane (see designated IP of FIG. 6). The image plane IP is located between the first and second lenses and at a predetermined distance from the first lens, which predetermined distance is defined by the focal length F1 of the first lens. After propagating through the image plane IP, the converging beam(s) form an equal one or more diverging beams that are received by the second lens. The second lens operates to receive the one or more diverging beams and to provide an equal number of collimated beams having predetermined angular displacements with respect to the optical axis 182 for directing or steering the collimated beams to predefined portions of the beam deflection device 188.

WO 2005/047813 PCT/US2004/029148 -24-

The telescope 193 is configured to provide a number of features, as described above, and further to convert diverging angular dispersion from the grating into converging angular dispersion after the second lens 192, which is desired for proper operation of the filter 170. In addition, the telescope 193 provides a useful degree of freedom, which controls the tuning range and reduces the beam size at the polygon mirror 194 to avoid a beam clipping.

5

10

15

20

As is illustrated in FIG. 6, the polygon mirror 194 reflects back preferably only the spectral component within a narrow passband as a function of the angle of the front mirror facet of the polygon with respect to the optic axis.

The reflected narrowband light is diffracted and received by the optical fiber 174.

The orientation of the incident beam with respect to the optic axis and the rotation direction 198 of the polygon mirror 194 determine the direction of wavelength tuning: wavelength up (positive) scan or down (negative) scan. The arrangement in FIG. 6 produces a positive wavelength sweep. It should be understood that while the mirror 194 is shown in FIG. 6 as having twelve facets, fewer or more than twelve facets can also be used. The particular number of facets to use in any application depends upon the desired scanning rate and scanning range for a particular application. Furthermore, the size of the mirror is selected in accordance with the needs of a particular application taking into account factors including, but not limited to, manufacturability and weight of the mirror 194. It should also be appreciated that lenses 190, 192 may be provided having different focal lengths. The lenses 190, 192 should be selected to provide a focal point at approximately the center point 200 of the mirror 194.

10

15

20

25

Consider a Gaussian beam with a broad optical spectrum incident to the grating from the fiber collimator 172. The well-known grating equation is expressed as  $\lambda = p \cdot (\sin \alpha + \sin \beta)$  where  $\lambda$  is the optical wavelength, p is the grating pitch, and  $\alpha$  and  $\beta$  are the incident and diffracted angles of the beam with respect to a nominal axis 202 of the grating, respectively. The center wavelength of tuning range of the filter is given by  $\lambda_0 = p \cdot (\sin \alpha + \sin \beta_0)$  where  $\lambda_0$  is the angle between the optic axis 38 of the telescope and the grating normal axis. It can be shown that FWHM bandwidth of the filter is given by  $(\delta\lambda)_{FWHM}/\lambda_0 = A \cdot (p/m)\cos \alpha/W$  where  $A = \sqrt{4 In 2/\pi}$  for double pass, m is the diffraction order, and W is  $1/e^2$ -width of the Gaussian been at the fiber collimator. When the real part of the complex spectral density is determined, ranging depth z is defined by  $z = \frac{\lambda_0^2}{4(\delta\lambda)_{FWHM}}$ .

Tuning range of the filter is fundamentally limited by the finite numerical aperture of lens1 20. The acceptance angle of lens1 without beam clipping is given by  $\Delta \beta = (D_1 - W \cos \beta_0 / \cos \alpha) / F_1$ , where  $D_1$  and  $F_1$  are the diameter and focal length of lens1. It relates to the filter tuning range via  $\Delta \lambda = p \cos \beta_0 \cdot \Delta \beta$ . An importance design parameter of the filter, originated from multiple facet nature of the polygon mirror, is the free spectral range, which is described in the following. A spectral component after propagating through lens1 20 and lens2 22 will have a beam propagation axis at an angle  $\beta'$  with respect to the optic axis 38:  $\beta' = -(\beta - \beta_0) \cdot (F_1 / F_2)$  where  $F_1$  and  $F_2$  are the focal lengths of lens1 and lens2, respectively. The polygon has a facet-to-facet polar angle given by  $\theta = 2\pi / N \approx L / R$  where L is the facet width, R is the radius of the polygon, and N is the number of facets. If the range of  $\beta'$  of incident spectrum is greater than the facet angle, i.e.  $\Delta \beta' = \Delta \beta \cdot (F_1 / F_2) > \theta$ , the polygon minor could retro-reflect more than one spectral component at a given time. The spacing of the multiple spectral components simultaneously reflected, or the free spectral range, can be shown to be  $(\Delta \lambda)_{FSR} = p \cos \beta_0 (F_2 / F_1) \cdot \theta$ .

10

15

20

25

30

In the application as an intracavity scanning filter, the tuning range of the laser cannot exceed the free spectral range if the gain medium has homogenous broadening, since the laser chooses the wavelength of highest gain. The duty cycle of laser tuning by the filter can be, in principle, 100% with no excess loss caused by beam clipping if two necessary conditions are met as follows:

$$W < \frac{\cos \alpha \ F_1}{\cos \beta_0 \ F_2} L \ and \ W < \frac{\cos \alpha}{\cos \beta_0} (F_2 - S) \cdot \theta \tag{17}$$

The first equation is derived from the condition that the beamwidth after lens 192 should be smaller than the facet width. The second equation is from that the two beams at the lowest and highest wavelengths 204, 206 respectively of the tuning range should not overlap each other at the polygon mirror S in Equation (1) denotes the distance between the lens 192 and the front mirror of the polygon.

In one experiment, optical components with the following parameters were selected: W=1.9mm, p=1/1200mm,  $\alpha=1.2$ rad,  $\beta_0=0.71$ rad, m=1,  $D_1=D_2=25$ mm,  $F_1=100$ mm,  $F_2=45$ mm, N=24, R=25mm, L=6.54, S=5mm,  $\theta$ =0.26rad,  $\lambda_0$ =1320nm. From the parameters, the theoretical FWHM bandwidth, tuning range and free spectral range of the filter could be calculated:  $(\delta\lambda)_{FWHM}=0.09$ nm,  $\Delta\lambda=126$ nm and  $(\Delta\lambda)_{FSR}=74$ nm. Both conditions in (1) are satisfied with margins. The characteristics of the filter were measured using broadband amplifier spontaneous emission light from a semiconductor optical amplifier (SOA) and an optical spectrum analyzer. The optical spectrum analyzer recorded the nonnalized throughput (reflected) spectrum in peak-hold mode while the polygon mirror was spinning at its maximum speed of 15.7 kHz. The measured tuning range was 90nm which is substantially smaller than the theoretical value of 126nm. The discrepancy was due to the aberration of the telescope, primarily field curvature, associated with relatively large angular divergence of the beam from the grating. It is expected that the aberration would be improved by using optimized lenses. The free spectral range was 73.5nm in agreement with the theoretical calculation. The FWHM bandwidth was measured to be 0.12nm. The discrepancy with theoretical limit of 0.11nm may be reasonable considering the aberration and imperfection of the optical elements.

10

15

FIG. 7 shows an extended-cavity semiconductor laser 208 according to an exemplary embodiment of the present invention which can include a filter 210 that may, for example, be similar to the filter 170 described above with reference to FIG. 6. The filter 210 is coupled through a light directing element 212 and a light path 214 to a Faraday circulator 216. In this exemplary embodiment, the filter 210 includes a grating 232 and a polygonal mirror 236. Thus, the filter 210 may correspond to a polygon-based filter. A motor 234 drives the mirror.

The Faraday circulator 216 of this exemplary embodiment is coupled through polarization controllers 220, 222 to a gain medium 224 which in one exemplary embodiment can be a semiconductor optical amplifier (e.g., SOA, Philips, CQF 882/e) having coupled thereto a current source 226 which provides an injection current to the SOA 224. The intracavity elements may be connected by single-mode optical fibers, for example. The two polarization controllers 220, 222 can align the polarization states of the intracavity light to align to the axes of maximum efficiency of the grating 232 and of maximum gain of the SOA 224.

A laser output 228 may be obtained through a 90% port of a fiber-optic fused coupler 230. To generate a sync signal useful for potential applications, 5% of the laser output may be coupled through a variable wavelength filter 237 having a bandwidth of 0.12nm and is directed toward a photodetector 238. In one exemplary embodiment, the center wavelength of the filter may be fixed at 1290nm. The detector signal generates short pulses when the output wavelength of the laser is swept through the narrowband passband of the fixed-wavelength filter. The timing of the sync pulse is controlled by changing the center wavelength of the filter.

FIG. 8A shows a graph 240 of an output spectrum of a laser of the type described above with reference to FIG. 7 as measured by an optical spectrum analyzer in peak-hold mode, when the polygon mirror (i.e. mirror 236 in FIG. 7) spins at a rate of 15.7 kHz. The edge-to-edge sweep range may be from l282nm to 1355nm over 73nm-width equal to the free-spectral range of the filter. The Gaussian-like profile of the measured spectrum, rather than a square profile, is likely due to the polarization-dependent cavity loss caused by polarization sensitivity of the filter and the birefringence in the cavity. It is preferable to adjust the polarization controllers to obtain the maximum sweep range and output power.

20

25

30

WO 2005/047813 -28-

5

10

15

20

25

30

FIG. 8B shows a curve 242 of a laser output in a time domain. The upper trace 244 corresponds to a sync signal obtained through the fixed-wavelength filter. The amplitude of power variation from facet to facet was less than 3.5%. The peak and average output power was 9mW and 6mW, respectively. It should be mentioned that the y-axis scale of curve 240 had to be calibrated from the time-domain measurement, because the optical spectrum analyzer only recorded a time-averaged spectrum due to the laser tuning speed much faster than the sweep speed of the spectrum analyzer.

PCT/US2004/029148

A frequency downshift in the optical spectrum of the intracavity laser light may arise as the light passes through an SOA gain medium (e.g. SOA 224 in FIG. 7), as a result of intraband four-wave mixing phenomenon. In the presence of the frequency downshift, the positive wavelength scan can facilitate tuning of the laser spectrum, and thereby produce higher output powers. The peak power of the laser output can be measured as a function of the tuning speed. The negative tuning speed may be obtained by flipping the position of the collimator and the orientation of the grating with respect to an optic axis (e.g., axis 182 in FIG. 6). It is preferable to make the physical parameters of the filter approximately identical in both tuning directions. Thus, the combined action of self-frequency shift and positive tuning allows higher output to be obtained and enables the laser to be operated at higher tuning speed. Therefore, the positive wavelength scan may be the preferred operation. The output power may decrease with increasing tuning speed. Thus, a short cavity length may be desired to reduce the sensitivity of the output power to the tuning speed. In this case, a free-space laser cavity is preferred.

FIG. 9A shows an exemplary embodiment of a free-space extended-cavity semiconductor tunable laser 250 according to an exemplary embodiment of the present invention that includes a semiconductor waveguide 252 fabricated on a substrate chip 254 coupled to a polygon scanning filter 255 through a collimating lens 256. A front facet 258 may be anti-reflection coated, and an output facet 260 is cleaved or preferably coated with dielectrics to have an optimal reflectivity. An output 262 of the laser is obtained through the output coupling lens 264. The collimating lenses 256, 264 are preferably provided as aspheric lenses.

WO 2005/047813 PCT/US2004/029148

The filter 255 includes a wavelength dispersing element 180' adapted to receive the beam directed thereto from the lens 256. The wavelength dispersing element 180' may be similar to wavelength dispersing element 180 described above with reference to FIG. 6. A lens system 186' can be disposed between the wavelength dispersing element 180' and a beam deflection device 188'. The wavelength dispersing element 180' and a beam deflection device 188' may be similar to wavelength dispersing element 180 and a beam deflection device 188 described above with reference to FIG. 6. The lens systems 186' includes a pair of lenses 187a, 187b which are preferably provided as achromats having low aberration particularly in field curvature and coma.

10

5

A sync output may be obtained by using a lens 266, a pinhole 268, and a photodetector 270 positioned on the 0-th order diffraction path for the light which is on retro-reflection from a polygon scanner 272. The detector generates a short pulse when the focus of the optical beam of a particular wavelength sweeps through the pinhole 268. Other types of gain medium may include, but are not limited to, rare-earth-ion doped fiber, Ti:Al<sub>2</sub>O<sub>3</sub>, and Cr<sup>4+</sup>:forsterite.

15

20

FIG. 9B, shows another exemplary embodiment of a wavelength tunable filter 280 according to the present invention which may include an optical fiber 281 coupled to an input collimating lens 282, optically coupled to a diffraction grating 284, a focusing lens 286, and a spinning disk 288. The diffraction grating 284 may be replaced by other angular dispersive elements such as a prism. In one exemplary embodiment, the diffraction grating 284 can have a concave curvature with a focal length selected such the focusing lens 286 is not needed.

25

30

Preferably more than one reflector 290 may be deposited on a surface 288a of the spinning disk 288. Preferably, the reflectors 290 comprise multiple narrow stripes periodically and radially patterned. The material for the reflectors is preferably gold. The disk 288 can be composed of a lightweight plastic or silicon substrate. Instead of the reflectors deposited on the top surface of the disk, the disk can have a series of through holes followed by a single reflector attached to the back surface of the disk. Incident from the optical fiber 281, the optical beams of different wavelengths may be illuminated on the surface of the disk into a line after being diffracted by the grating and focused by the lens 286 (in those

systems which include lens 286). Preferably, only the beam that impacts the reflectors of the spinning disk may be retro-reflected and received by the optical fiber 281. A mirror 292 may be used to facilitate the access of the beam onto the disk.

5

The distance from the lens 286 to the reflectors of the disk 288 is equal to the focal length, F, of the lens. It can be shown from the grating equation that the tuning range of the filter is given by  $\Delta \lambda = p\cos \beta_0 (D/F)$  where D denotes the distance between the stripes. The width of the strip, w, is preferably made to be substantially equal to the beam spot size  $w_s$ , at the surface of the disk:

10

$$w_S = W \frac{\cos \beta_0}{\cos \alpha} \cdot \frac{F/z}{\sqrt{1 + (f/z)^2}}$$
 where  $z = \pi w_s^2 / \lambda$ . It leads to a FWHM filter

bandwidth given by  $(\delta\lambda)_{FWHM}/\lambda_0 = A\cdot(p/m)\cos\alpha/W$  where  $A = \sqrt{4\ln2/\pi}$ . For the  $w>w_s$ , filter bandwidth becomes greater, and for  $w< w_s$ , the efficiency (reflectivity) of the filter is decreased by beam clipping. The orientation of an incident beam 294 with respect to the optic axis of the lens 286 and the spinning direction 288 preferably determines the sense of wavelength tuning. The positive wavelength scan is preferable, which is achieved by spinning the disk 288 in a clockwise direction as shown in FIG. 9B.

## a. Interferometer

20

15

FIG. 10A shows an exemplary embodiment of an OFDI system 300 according to the present invention for performing optical imaging using frequency-domain interferometry includes a frequency swept source 301 which emits a light signal having an instantaneous emission spectrum comprised of a plurality of frequency modes of the light source. Source 301 may, for example, be provided as one of the sources described above with reference to FIGS. 4A, 5, 6, 7, 9 and 9B. The light from source 301 can be directed toward a fiber-optic coupler 302 which divides the light fed thereto into a reference arm 303 and a sample arm 304.

30

25

The reference arm 303 preferably includes a polarization circuit 306 and a circulator 308. Thus, light propagates from source 301 through the coupler 302, the polarization circuit 306 and the circulator 308 to an optional motion

artifact circuit 309. The optional motion artifact circuit 309 may be provided from a lens 310 which directs the light toward a frequency shifter 311, a phase tracker 312 and a dispersion compensator 314. The light passes through optional circuit 309 and is incident upon a reference mirror 316. It should be appreciated that circuit 309 functions to remove or reduce motion artifacts. It should also be appreciated that circuit 309 may include all of the elements 310-314, and/or one or more of the circuit elements 310-314.

The sample arm 304 may include a circulator 318. Thus, a light signal transmitted from the source 301 propagates from source 301 through the coupler 302 and the circulator 308 to a lens 320 which directs the light toward a scanning mirror 322. The scanning mirror 322 may be provided from a wide variety of optical elements including but not limited to, a galvanometer, a piezoelectric actuator or another functionally equivalent device. A transverse scanner 324 is coupled to the scanning mirror 322 and a data acquisition board and computer 326. The data acquisition board and computer 326 is also coupled to the frequency swept source 301.

The OFDI system 300 shown in FIG 10A can also include a polarization diversity balanced detection ("PDBD") circuit 334 configured to receive signals from the reference arm 303 and/or the sample arm 304. In particular, the reference arm 303 is connected through circulator 308 and polarization control circuit 330 to a reference port of the PDBD circuit 334. Similarly, sample arm 304 is connected through circulator 318 and polarization control circuit 332 to a sample port of the PDBD circuit 334.

# 25 b. <u>Interferometer</u>

5

10

15

20

30

The sample arm 304 collects light reflected from a tissue sample 328 and is combined with the light from the reference arm 303 in the polarization diversity balanced detection (PDBD) circuit 334 to form interference fringes.

For example, the OFDI technique does not require that the optical path length in the reference arm be scanned in time. Thus, in certain exemplary embodiments of the present invention, it may be preferable to provide the reference arm as a fixed delay reference arm. Such fixed delay reference arms

may have various configurations that are known to those having ordinary skill in the art.

The reference arm 303 can be either of reflective and/or transmission type, and can return light back from the mirror 316. The returned light is directed toward the polarization control circuit 330 via the circulator 308. Similarly, the reflected light from the sample 338 can be directed toward a polarization control circuit 332 via the circulator 318. The reference arm can also be transmission with no reflection. The polarization control circuit 330 can be used to match the polarization state of the reference-arm light to that of the sample-arm. The total birefringence in the interferometer should be minimized not to induce wavelength-dependent birefringence. The polarization controller may include, but is not limited to, a fiber-optic polarization controller based on bending-induced birefringence or squeezing.

Preferably, the chromatic dispersion should be matched substantially between the reference and sample arm. The result of strong dispersion mismatch may be a loss in the axial resolution. Any residual dispersion can likely be compensated by appropriate signal processing, such as nonlinear mapping based on interpolation of the detector data before the Fourier transform. This mapping may also be accomplished, at least in part, by adjusting the optical layout of the wavelength-swept source. In one example in which the source 301 includes a polygon scanner and a telescope, the distance between the polygon scanner and the telescope can be adjusted to convert wavelength space to wave vector space prior to Fourier transformation.

#### c. Sample arm

5

10

15

20

30

For certain OFDI applications, the sample arm may be terminated by an optical probe comprising a cleaved (angled, flat, or polished) optical fiber or free space beam. A lens 336 (such as, but not limited to, aspherical, gradient index, spherical, diffractive, ball, drum or the like) may be used to focus the beam on or within the sample. Beam directing elements (such as, but not limited to, mirror, prism, diffractive optical element or the like) may also be contained within the probe to direct the focused beam to a desired position on the sample. The position of the beam may be changed on the sample as a function of time,

WO 2005/047813 PCT/US2004/029148

allowing reconstruction of a two-dimensional image. Altering the position of the focused beam on the sample may be accomplished by the scanning mirror 322. The scanning mirror 322 may be provided, for example, from a number of different devices including, but not limited to, a galvanometer, piezoelectric actuator, an electro-optic actuator or the like.

The sample arm probe may be a fiber optic probe that has an internally moving element, such that the motion is initiated at a proximal end of the probe and the motion is conveyed by a motion transducing arrangement (such as, but not limited to, wire, guidewire, speedometer cable, spring, optical fiber and the like) to the distal end. The fiber optic probe may be enclosed in a stationary sheath which is optically transparent where the light exits the probe at the distal end. Thus, scanning way also be accomplished by moving the optical fiber. For example, by rotating the optical fiber, or linearly translating the optical fiber. FIG. 10B shows an exemplary embodiment of the probe 359 which includes an inner cable 360 (that may rotate or linearly translate along the axis of the probe), an outer transparent or semi-transparent sheath 362, distal optics 364, and remitted light 366 (which may be at any angle with respect to axis of catheter).

### d. Detection

20

25

5

10

15

The PDBD circuit 334 may include a plurality of detectors 370 disposed to provide dual balanced detection. Dual balanced detection may be preferred in certain applications for the following reasons. First, most light sources generate I/f noise (f = frequency) at relatively low frequencies and balanced detection will eliminate I/f source noise. Second, an interference term of the sample arm light with itself (i.e. an auto-correlation term) can be present on top of the true signal term, which is preferably the interference between sample and reference arm. Such auto-correlation term can be eliminated by a differential technique and balanced detection may eliminate this auto-correlation term from the measured signal. Third, RIN can be reduced.

30

The detectors 370 may preferably include photodiodes (such as, but not limited to, silicon, InGaAs, extended InGaAs, and the like). Balanced detection can be implemented by subtracting diode signals that are exactly out of phase with respect to the maxima and minima pattern. The difference between

two detector signals is obtained by a differential circuit included in PDBD circuit 334 and amplified by trans-impedance amplifiers ("TIA") 360. The dual balanced receiver may be further followed by a low-pass or band-pass filter to reject noise outside the detection bandwidth.

5

10

In this exemplary embodiment of the present invention, the dual balanced detection can be implemented as follows. The polarization beam splitter 362 receives signals from the reference and sample arms and provides two output signals. The two output signals are further split by two non-polarizing beam splitters 364a, 364b, respectively. The outputs from each beam splitter 364a, 364b are detected by a dual balanced receiver provided from the four detectors 370. Furthermore, the two outputs of the dual balanced receivers are digitized and processed in a computer arrangement to obtain a polarization diversity.

15

The receiver output is provided to circuit 326 which acquires and digitizes the signals fed thereto via A/D converters, and stores the digitized signals in a computer for further processing. The bandwidth of the TIA is preferably matched to half the sampling rate. Gain of the TIA is preferably selected such that the maximum receiver output range is matched to the voltage range of the A/D converter.

# e. Processing

If more than two detectors are used, the signals can be selectively subtracted and complex spectral density can be obtained. Using the Fourier transform, the complex cross spectral density can be converted to a depth profile in the tissue. Several methods to process the complex spectral density to obtain depth profile information are known to those skilled in the art, such as, but not limited to, by obtaining at least two signals with a Pi/2 phase shift in the reference arm and then reconnecting the complex spectral density by some linear combination of the two signals, or by squaring the spectral density.

30

25

Following the detection, analog processing can include a transimpedance amplifier, low pass (band pass) filter, and digitization of the signal.

This signal may then be converted to reflectivity as a function of depth by the
Fourier transform operation. Digital processing includes digitization, digital band
pass filtering in either the frequency domain or time domain (FIR or IIR filter) and

inverse Fourier transformation to recover the tissue reflectivity as a function of depth.

Prior to the Fourier transformation, the detected non-linear wavelength coordinates is preferably converted to regularly sampled wave-vector space.

Typically zero padding the signal, Fourier transformation, and inverse Fourier transformation with re-sampling can be utilized for remapping. Other interpolation methods known in the art, such as linear, bi-linear, and cubic spline interpolation of the data may also be used to convert wavelength space into regularly sampled k space. This mapping may also be accomplished in part by adjusting the optical layout of the wavelength-swept source. In one example, the distance between the polygon scanner and the telescope may be adjusted to convert wavelength space to wavevector space prior to Fourier transformation.

Another exemplary embodiment of the present invention can utilize one or more techniques described below to further enhance the performance and functionality of imaging. These techniques are not limited to the OFDI techniques that use a multiple-frequency-mode tuned source, but can be applied in the OFDI technique using a single-frequency tuned source.

#### a. Polarization diversity

20

25

30

5

10

15

For an application where polarization fading is a problem, a polarization diversity scheme may be used. Various configurations for polarization diversity are known in the art.

In the system shown in FIG. 10A, the polarization diversity circuit operates as follows. The polarization beam splitter 362 separates the reference-arm and sample-arm light signals depending upon their polarization states. The polarization controller 330 is preferably adjusted so that the reference-arm power is split with an equal magnitude by the polarization controller. The polarization state of the sample arm power can be assumed to vary randomly due to the probe or sample motion, therefore the separating ratio of the sample arm power by the polarization splitter can vary in time. However, the two output signals at the two output ports of the polarization beam splitter 362 can be detected by a photo receiver, e.g., squared and summed. The resulting signal is independent of the polarization state of the sample arm light.

WO 2005/047813 PCT/US2004/029148 -36·

## b. Carrier-frequency heterodyne detection

5

10

15

20

25

30

The optical frequency shifter 311 may be situated in the reference arm 303 to shift the optical frequency for carrier-frequency heterodyne detection. As a result, the signal frequency band is shifted by the magnitude of the frequency shift. In this manner, relatively large 1/f noise (f = f frequency) and RIN around DC can be avoided. The frequency shifter can be, but not limited to, an acousto-optic frequency shifter. In the detection, a proper electronics should be used to demodulate the carrier frequency.

One of the benefits of using the frequency shifter 311 is that the effective ranging depth can be doubled. This can be illustrated in the electrical frequency domain, as shown in FIG. 10C in which a graph 380 depicts the fringe visibility curve given by the instantaneous output spectrum of the source. The visibility curve has a Gaussian profile if the source's instantaneous spectrum is Gaussian. A curve 390 depicts the transmission efficiency profile of an electrical filter, which is optimized for a given Nyquist frequency defined as the half of the sampling frequency. Section (a) of FIG. 10C shows a typical case where there is no frequency shifter in the interferometer and the electrical filter is a low pass filter. Because the positive and negative frequency band is not differentiable, the images associated with the positive and negative frequency band, respectively, are overlapped. Because of this ambiguity, only half of the frequency range (zero to  $f_N$ ) or (zero to  $-f_N$ ) is usable in this case. However, using a frequency shifter results in a shift of the visibility curve by  $f_{\rm FS}$ , as shown in portion (b) of FIG. 10C. With a bandpass filter (or a low pass filter), both sides of the frequency band centered at f<sub>FS</sub> produce images without ambiguity, resulting in a twice larger ranging depth compared to section (a) of FIG. 10C.

Instead of a square-top bandpass filter, it is possible to use a slope filter. In an example shown in FIG. 10C section (c), the transmission efficiency curve of the filter, 390, has an exponentially-rising (falling) slope in its low frequency band. This filter may be useful in which attenuation is significant and the resulting signal strength decays with depth. The slope filter can improve the dynamic range of the detection by effectively suppressing the large signal from the surface relative to that at greater depths.

## c. Reference arm delay (Phase tracking and Auto-ranging)

As described above, the OFDI technique does not :require the optical path length in the reference arm to be scanned in time. A fixed-delay reference arm can be made in various configurations that are known to those having ordinary skill in the art. The reference arm can be of either reflective or transmission type.

In certain applications, the capability of varying the optical delay in the reference arm may be useful when a larger ranging depth is desired, without increasing the data acquisition rate or reducing the instantaneous linewidth of the optical source. Such ability is useful in a clinical study where the distance from the imaging lens and the front surface of the sample can varies significantly. Such variation can result from the motion or from the uncontrolled position of a probing catheter. For example, a rotating catheter inside a blood vessel can have distance variation by a couple of millimeter over a single A-scan.

15

20

25

30

10

5

A mechanism in the reference arm 303 may allow for scanning the group delay of the reference arm 303. This group delay can be produced by any of a number of techniques known to those having ordinary skill in the art, such as, but not limited to, stretching an optical fiber, free space translational scanning using a piezoelectric transducer, or via a grating based pulse shaping optical delay line. Preferably, the delay can be introduced by a non-mechanical or motionless arrangement. By the term "non-mechanical", what is meant is that there are no mechanically moving parts being utilized. The absence of the mechanically moving parts is believed to reduce the known deficiencies of using mechanical devices to introduce delay. In contrast to traditional LCI or OCT systems, the reference arm 303 according to an exemplary embodiment of the present invention does not necessarily need to scan over the full ranging depth in the sample, and can preferably scan over at least a fraction of the ranging depth equal to one over the number of detectors (1/N). This scanning feature is different from the conventional delay scanning schemes used in the known LCI and OCT systems. The reference arm 303 optionally has a phase modulator mechanism. such as but not limited to, an acoustooptic modulator, electro-optic phase modulator or the like, for generating a carrier frequency.

PCT/US2004/029148

5

10

15

20

25

30

Phase tracking is preferable performed to eliminate phase instabilities in the interferometer. Phase instabilities can cause individual interferometric fringes to shift in location. If detection is slow relative to the shifting of the fringes, the resulting averaging results in chirping of the interference signal. Ascan rate of 10 to 40 kHz results in an effective integration time of 100 to 25 µs. Phase instabilities arising on a time frame shorter than the integration time should be compensated. Phase locking circuitry is commonly used in electronics, and is frequently used in radar and ultrasound. Active phase tracking can be implemented by modulating the interferometer path length difference at 10 MHz with an electro-optic phase modulator in the reference arm over a fraction of the wavelength. By demodulating the intensity measured by one detector at the output of the interferometer at the frequency of the path length modulation, an error signal can be generated indicating in which direction the phase modulator should shift to lock onto a fringe amplitude maximum. By adding an offset to the phase modulator as determined by the error signal, the phase tracker actively locks onto a fringe maximum.

The phase modulator can modulate the path length difference over a few wavelengths. The processing unit can determine if the phase modulator has reached its range limit, and jump by a full wave in phase to maintain lock on a different fringe maximum. This approach exploits the fact that phase should be controlled only modulo  $2\pi$ . In addition, the processing drives a slower component (e.g., the Rapid Scanning Optical Delay ("RSOD") line) to extend the path length range of the phase modulator/RSOD combination over several millimeters. Phase locking can be performed on a fringe maximum, minimum, or zero crossing, based on the type of mixing performed in the demodulation circuit.

Another exemplary embodiment of the present invention can also use autoranging techniques and technology, including processing techniques described in U.S. patent application publication no. 2002/0198457, the disclosure of which is hereby incorporated herein by reference in its entirety. The autoranging mechanism may, in one exemplary embodiment, include a processor unit for (a) obtaining a first scan line; (b) locating a surface location "S" of a sample; (c) locating an optimal scan range "R" of the sample; (d) modifying a reference arm

5

10

15

20

25

30

delay waveform to provide an output; (e) outputting the output to a reference arm; (f) determining whether the image is complete; and/or (g) moving to the next scan line if the image is not complete or remapping the image using the surface S data and the waveform data stored in the memory storage device if the image is complete.

If the light signal returned from the sample has a low amplitude, phase locking may be unstable due to the presence of noise. In another exemplary embodiment of the present invention, a separate, preferably monochromatic, light source can be transmitted into the interferometer. The separate source wavelength may be within the wavelength tuning range of the OFDI source or may be centered at a different wavelength than the OFDI source spectrum. The separate source is preferably of higher power, and may be combined with the source arm (using wavelength division, multiplexer, grating, prism, filter or the like) travel to the reference and sample arms and return back to the beam recombining element. The returned separate source light can then be separated from the OFDI light following transmission back through the beam recombining element (i.e. beam splitter output). A separation arrangement can perform spectral separation by a dispersing element, such as a dichroic mirror, filter, grating, prism, wavelength division multiplexer or the like. The separate source will be detected separately from the OFDI light using one or more detectors. The higher power provided by this separate source can enable detection of a higher amplitude interference pattern, and provide an improved input to the phase tracker, thus enabling more stable phase tracking.

Referring now to FIG. 11, an *in vivo* image of a subject's fingertip (300\*500 pixels) acquired at an A-line scan rate of 15.7 kHz is shown using the exemplary embodiment of the system and process according to the present invention. The optical sensitivity was measured to be about -100 dB. The SNR is superior to an equivalent TD OCT of the same A-line scan rate. The vertical line noise arises due to an un-optimized detection when there is a strong mirror-like reflection from the surface of the tissue, but should preferably be eliminated substantially by a detection optimization and/or an appropriate signal processing.

FIG. 12 shows another exemplary embodiment of a phase tracker system 600 according to the present invention having an extended phase lock

5

10

15

25

range is provided. This done by combining a fast element 602 (which may be provided, for example, as an electro-optic (EO) phase modulator 602) to modulate the path length difference over a small range, and a slower element 604 (which may, for example, be provided as a Rapid Scanning Optical Delay (RSOD) line 604) to modulate the path length over an extended range. The detector 606 signal can be mixed with the phase modulator modulation frequency 608 by a mixer 610 and low pass filtered (filter not shown) to generate an error signal. The processing unit 612 preferably processes the error signal to generate an offset voltage, and adds this offset voltage to the modulation signal 608, so as to generate the output for the phase modulator driver 614. In addition, the processing unit 612 can generate a signal to the RSOD 604 to provide extended range tracking of the phase over distances of several millimeters. Light source 616, fiber splitter 618, sample arm 620 and reference arm 622 are shown, and are described herein.

The intensity I(t) at the detector at a given moment within a single oscillation of the fringe pattern is given by

$$I(t) = \cos \left[\phi(t)\right]$$

where the phase  $\varphi$  gives the position in the fringe. For  $\varphi=0$ , the signal is at a fringe maximum, for  $\varphi=\pi$ , the signal is at a fringe minimum. At an arbitrary moment t, the phase  $\varphi(t)$  is given by,

$$\phi(t) = \alpha + \beta \sin(\omega t)$$

where  $\alpha$  describes the position within a single oscillation of the fringe pattern, and  $\beta$ \*sin( $\omega$ t) is the phase modulation introduced by the phase modulator, with  $\beta$  the amplitude of the phase modulation, and  $\omega$  the frequency of the phase modulation signal. The intensity at the photodetector I(t) can be mixed with a carrier at frequency  $\omega$  and  $2\omega$ , resulting in the mixer signal MixerC(t), MixerS(t), Mixer2 $\omega$ C(t) and Mixer2 $\omega$ S(t).

$$MixerC(t) = \cos(\omega t) * \cos(\alpha + \beta \sin(\omega t));$$

$$MixerS(t) = \sin(\omega t) * \cos(\alpha + \beta \sin(\omega t));$$

$$Mixer 2\omega C(t) = \cos(2\omega t) * \cos(\alpha + \beta \sin(\omega t));$$

30 
$$Mixer 2\omega S(t) = \sin(2\omega t) * \cos(\alpha + \beta \sin(\omega t))$$
.

5

10

15

20

25

30

WO 2005/047813 PCT/US2004/029148

The time average over a single oscillation of the carrier frequency  $\omega$  of MixerC, MixerS, Mixer2 $\omega$ C and Mixer2 $\omega$ S is given by,  $\overline{MixerC(t)} = 0$ ;  $\overline{MixerS(t)} = \sin(\alpha) * J_1(\beta); \overline{Mixer2\omega C(t)} = \cos(\alpha) * J_2(\beta); \overline{Mixer2wS(t)} = 0$ where  $J_1(\beta)$  and  $J_2(\beta)$  are a Bessel functions of the first kind; its value depends on  $\beta$ , the amplitude of the phase modulation. Thus, the signal  $\overline{\textit{MixerS(t)}}$  and  $\overline{Mixer2\omega C(t)}$  are proportional to  $\sin(\alpha)$  and  $\cos(\alpha)$ , respectively, with  $\alpha$  the position within a single oscillation of the fringe pattern. The mixer outputs MixerS(t) and  $Mixer2\omega C(t)$  are used as an error signal to generate an offset voltage to steer the phase modulator to a new center position that minimizes the error signal, and locks the interferometer output on a fringe maximum or minimum, or a zero crossing, respectively. The complex spectral density can now be determined by two consecutive tuning scans, one where the error signal  $sin(\alpha)$ is minimized, and the next where the error signal cos(a) is minimized, resulting in a 90 degrees phase shift between the two interference patterns. Using this mixing arrangement, the complex spectral density can be obtained rapidly and without resorting to an additional mechanical arrangement for changing the phase of the reference arm light.

Fig. 13 shows a further exemplary embodiment of an OFDI system 700 which includes a phase tracker for providing balanced detection according to the present invention. In this exemplary embodiment, a source 702 provides an electro-magnetic radiation (e.g., light) which passes through a splitter 704, that sends part of the light to a sample probe 706 and the remainder of the light to a Rapid Scanning Optical Delay ("RSOD") line 708. Light is passed from the RSOD 708 to the phase modulator PM 710. Light from the phase modulator PM 710 is transmitted through a splitter 712, and then through two additional splitters 714 and 716, a portion of the output of which is sent as balanced detection outputs to spectral detection units (not shown, but as described elsewhere herein) and the remainder of the output is sent to the phase tracker assembly 720. In the phase tracker assembly 720, phase tracker detectors  $D_1$  and  $D_2$ , 722 and 724, receive the partial output of the pair of splitters 714 and 716, which in turn send signal to a

mixer 726 to generate an error signal. A processing unit 728 processes the error signal, where the sum generation of offset voltage and adds this to the modulation signal 730 to generate the output for the phase modulator driver 732. Modulation signal, shown at box 730, is forwarded to the mixer 726 and the processing unit 726. In addition, the fringe amplitude could be too small for the phase tracker to lock. Alternatively, a secondary source with longer coherence length can be coupled to the system 700, e.g., to provide a larger fringe amplitude to the phase tracker.

5

10

15

20

25

30

FIGS. 14A-14C show an exemplary embodiment of a method for tracking phase in an imaging system begins in processing blocks 750 and 752 according to the present invention by measuring a signal received from the sample arm and then increasing a phase of the signal. Processing of this exemplary method then proceeds to block 754, in which a first signal partition of the signal defined as  $x_1$  is measured at least one peak of the signal. In decision block 756, a determination is as to whether the signal defined as  $x_1$  has been measured at least one peak of the signal. If in decision block 756, it is determined that the signal defined as  $x_1$  has been measured at least one peak of the signal, then processing returns to block 754 and the signal is again measured.

On the other hand, if in decision block 756, it is determined that the signal defined as  $x_1$  has not been measured at at least one peak of the signal, then processing flows to a decision block 758, where a determination is made as to whether to adjust the signal. The adjustment may be, e.g., an increase or a decrease in the phase of the signal by an incremental amount as shown in blocks 760 and 762. Regardless of whether an increase or a decrease in the phase of the signal is made, processing returns to processing block 754, where a second signal partition of the signal is measured at its peak. Blocks 756-762 are then repeated for such measured signal. It should be noted that the functions of blocks 750-762 may be performed in parallel and/or series with other imaging processes.

The adjustment of phase " $\phi$ " can be defined as  $A(x_2-x_1)$ , where "A" is a constant and that the process of determining whether to increase or decrease the phase of the signal by an incremental amount may further comprise the substeps of (1) determining whether  $A(x_2-x_1)$  is within range of the phase modulator; and (2) changing  $\phi$  by an amount equal to  $A(x_2-x_1)$  if  $A(x_2-x_1)$  is within the range or

WO 2005/047813 PCT/US2004/029148 -43-

changing  $\varphi$  by an amount equal to  $A(x_2-x_1)-m2\pi$  if  $A(x_2-x_1)$  is outside of the range, where M is an integer greater than 1. The method may optionally further comprise a substep (3) re-measuring signal  $x_1$ .

# d. Data processing

5

10

15

20

25

30

In general, the data recorded by the detector in time may not be sampled as a strictly linear function of the optical frequency  $\omega$  or wave number k. The Fourier transform, however, can link z and k space (or t and  $\omega$ ). Because of the non-linear sampling in k, the acquired spectrum is interpolated to create evenly spaced samples in the k domain. Alternatively, the tuning slope of the laser could be adjusted in such a way that the light is samples in equal intervals in k space, such that the interpolation becomes obsolete. Alternatively, the detection timing could be designed to sample the light evenly spread in the k domain, such that the interpolation becomes obsolete. To achieve the optimal point spread function, dispersion in the sample and reference arm of the interferometer should preferably be balanced. Dispersion imbalance can also be corrected by digital processing. Phase chirping induced by motions can also be corrected by digital processing. For the motion artifact correction, the axial movement of the sample is measured, and a proper nonlinear mapping can be calculated from the velocity of the movement.

Various interpolation techniques are known to those having ordinary skill in the art. This includes, but is not limited to, simple two-point interpolation, FFT zero-padding followed by two-point interpolation, and rigorous interpolation with the sinc function dictated by the Nyquist theorem.

An exemplary embodiment of the present invention may also provide a probe for locating atherosclerotic plaque in a blood vessel, comprising: an interferometer; a spectral separating unit which splits signal received from the interferometer into a plurality of optical frequencies; and a detector arrangement capable of detecting at least a portion of the optical frequencies received from the spectral separating unit.

### e. Frequency shifting technique

For high-speed OFDI techniques, the maximum ranging depth can likely be limited by the finite width of the coherence function of the laser output because the coherence length is often compromised to obtain higher tuning speed, higher output power, or wider tuning range. The finite coherence length may cause the visibility of the interference fringe to decrease as the path length difference of the interferometer increases. This result in the degradation of SNR, and therefore limits the maximum ranging depth. Furthermore, the inability to distinguish between a positive and negative electrical frequency in a conventional interferometry may lead to the ambiguity between positive and negative depths. To avoid the imaging folding artifact, the reference delay of the interferometer should be adjusted so that the image presents at only either positive or negative depth. This further may limit the ranging depth for a given coherence length of the source.

15

20

10

5

To avoid such possible limitation, quadrature interference signals have been measured based on active or passive phase biasing using a piezoelectric actuator, birefringence plate or 3x3 coupler. These techniques may provide otherwise overlapping images associated with positive and negative depths, but tended to leave significant residual artifacts due to the difficulty of producing stable quadrature signals. In this paper, we propose and demonstrate a simple technique that effectively eliminates the ambiguity between positive and negative depths.

25

30

The exemplary technique according to the exemplary embodiment of the present invention uses an optical frequency shifter in the interferometer to provide a constant frequency shift of the detector signal. This allows both sides of the coherence range to be used without crosstalk, and can double the ranging depth. The same concept has been described above in the context of 1-dimensional optical frequency domain reflectometry using rotating birefringence plates at 58 Hz or a recirculating frequency shifting loop. In this exemplary embodiment, an acousto-optic frequency shifter is used, and the technique is applied to high-speed OFDI with several orders of magnitude faster ranging speed. Furthermore, a signal processing technique according to a further

exemplary embodiment of the present invention is provided to accommodate a nonlinear tuning slope of the swept source in the frequency shifting technique.

# A. Principle

5

10

15

25

30

## Frequency shift

FIG. 15 shows a high level diagram of the OFDI system according to the present invention which includes a wavelength-swept source 95, singlemode-fiber interferometer employing an optical frequency shifter 311 in a reference arm 80, a photodetector 88, and a signal processor 160. With a roundtrip frequency shift of  $\Delta f$  in the reference arm, the photocurrent associated with the interference between the reference and sample light can be expressed as

$$i_s(t) = \eta \sqrt{P_r(t)P_s(t)} \int \sqrt{R(z)} G(|z|) \cos\left[\frac{4\pi}{c}v(t)z + \phi(z) + 2\pi \Delta f t\right] dz,$$

where  $\eta$  denotes the quantum efficiency of the detector, Pr(t) and Ps(t) the optical powers of the reference and sample arm light, respectively, R(z) the reflectivity profile of the sample, G(|z|) the coherence function corresponding to the fringe visibility, c the speed of light, v(t) the optical frequency, and  $\phi(z)$  the phase of backscattering. In the case of a linear tuning, i.e. v(t) = 0 - 1t, the frequency of the detector signal is given by

$$f_x = |v_1 \frac{2z}{c} - \Delta f|$$

The zero signal frequency corresponds to a depth  $z = c\Delta f/(2 v1)$ .

Therefore, by choosing the direction of frequency shifting same as the tuning direction of the swept source, the zero signal frequency can be made to point to a negative depth. FIGS. 16(a) and 16(b) illustrate the effect of the frequency shift. The fringe visibility or the coherence function has a peak value at the zero depth and decrease as the depth increases. The coherence length  $z_c$  indicates the depth where the visibility drops to 0.5 and thereby the SNR drops by 6 dB. One may arguably define the effective ranging depth as the maximum depth span where the SNR penalty is less than 6 dB. For example, in FIG. 16(a), a single side of the coherence range can be used due to the sign ambiguity of the signal frequency (hatched region). In contrast, as shown in FIG. 16(b), with an appropriate

WO 2005/047813 PCT/US2004/029148 -46-

frequency shift, both sides of the coherence range from  $-z_c$  to  $z_c$  can be utilized without any image crosstalk between the negative and positive depths.

#### Nonlinear tuning

5

10

Nonlinearity in v(t) with respect to time results in frequency chirping of the signal at a constant depth and causes the degradation of axial resolution. As a solution to this problem, the detector signal may be sampled with nonlinear time interval compensating for the frequency chirping. Alternatively, the detector signal can be sampled with a constant time interval, and then the sampled data be mapped to a uniform v-space by interpolation prior to discrete Fourier transform ("DFT"). Both methods have been demonstrated to yield a transform-limited axial resolution. However, these methods are not applicable directly in the frequency shifting technique. Both the nonlinear sampling and interpolation method can result in artificial chirping of the frequency shift, leading to sub optimal axial resolution. Thus, a modified interpolation method can be used to achieve nearly transform-limited axial resolution over the entire ranging depth. The exemplary technique may be as follows:

- 15
- Step 1. Obtain N samples of the signal with uniform time interval during each wavelength sweep of the source.

20

- Step 2. Produce DFT of N data points in the electrical frequency domain.
- Step 3. Separate two frequency bands below and above  $\Delta f$  corresponding to negative and positive depths, respectively.
- Step 4. Shift each frequency band such that the zero depth is aligned to the zero electrical frequency.

25

Step 5. Apply zero-padding to each frequency band and perform inverse DFT resulting in an array of increased number of samples in the time domain with smaller time interval for each frequency band.

30

Step 6. Interpolate each array in the time domain into a uniform v space using a proper mapping function given by the nonlinearity of the swept source.

- Step 7. Conduct DFT of each interpolated array.
- Step 8. Combine the two arrays (images) by shifting the array index.

As a result, the zero depth lies at the electrical frequency of  $\Delta f$ .

FIG. 17 depicts the experimental setup of an exemplary OFDI system

## B. Experiment

#### **OFDI System**

10

5

employing two acousto-optic frequency shifters (FS1 800 and FS2 802, Brimrose Inc. AMF-25-1.3) according to an exemplary embodiment of the present invention. The two frequency shifters may be driven with voltage controlled oscillators to produce a net shift of  $\Delta f = FS2 - FS1$ . The use of two frequency shifters balanced the material dispersion of the acousto-optic crystals automatically. The insertion loss of each device including fiber coupling may be less than 2.5 dB. The sampling rate of the digitizer can be 10 MHz. The swept laser 100 may be constructed to provide a tuning range of 108 nm centered swept from 1271 nm to 1379 nm (  $\nu l$  = 135 GHz/ $\mu s$ ). Although a repetition rate up to 36 kHz could be achieved, the laser was operated at a reduced rate of 7 kHz and 1300 samples were acquired during a single wavelength sweep. This resulted in a depth span of 5.8 mm in the image corresponding to the Nyquist frequency of 5 MHz. The probe 810 may include a galvanometer mirror and an imaging lens produced a probe beam with a confocal parameter of 1.1 mm. An optical tap coupler 820 can be used in conjunction with a narrowband filter 830 and a photodetector 834 to generate a TTL trigger signal in an electrical circuit 836. The TTL signal may be used as a trigger in analog to digital conversion.

20

15

The interference signal can be measured using a dual balanced receiver 151. The detector signal was further processed prior to digitization using a low pass electrical filter 840. Other types of electrical filters such as a band pass filter and a slope filter. The transmission of the slope filter may have an exponentially-rising (falling) slope in its low frequency band. This filter may be useful in which attenuation is significant and the resulting signal strength decays with depth. The slope filter can improve the dynamic range of the detection by effectively suppressing the large signal from the surface relative to that at greater depths.

30

25

To characterize the coherence function of the swept laser 100, the point spread function of the system may be measured at  $\Delta f = 0$  (FS1 = -25 MHz, FS2 = -25 MHz) with a partial reflector at various locations of the reference mirror. For

comparison, the sampled data acquired at each depth was processed with and without the mapping process. FIGS. 18(a) and 18 (b) show exemplary results, where the y-axis represents the square of the DFT amplitudes normalized to the value at zero frequency, and the bottom and top x-axes represent the signal frequency and the depth z, respectively. Without mapping, the point spread function suffers from significant broadening and large degradation of the peak power as the depth increases, because of the nonlinearity of our swept laser [see FIG. 18(a)]. With the mapping process, however, the spread function exhibits nearly transform-limited axial resolution as shown in FIG. 18(b). The finite coherence length of the laser output accounts for the decrease of the signal power depth. Over the entire depth span of 5.8 mm, the SNR is reduced by more than 11 dB. According to the criterion for the effective ranging depth introduced earlier, the depth corresponding to the coherence length may be only 2.9 mm, a half the total in the image. The same experiment was conducted with a nonzero frequency shift of  $\Delta f = -2.5$  MHz (FS1= -22.5 MHz, FS2 = -25 MHz). FIGS. 18(c) and 18(d) show the point spread functions measured with and without the mapping process, respectively. As shown in these figures, the peak of the signal power occurring at the zero depth present at a frequency of 2.5 MHz is at least approximately equal to the net acousto-optic frequency shift. The nearly transform-limited axial resolution observed in FIG. 18(d) validates the mapping technique. The reduction in the signal power is less than 5 dB over the entire depth span of 5.8 mm, demonstrating the benefit of the frequency shifting technique in terms of extending the ranging depth.

# 25 Image

5

10

15

20

30

Exemplary imaging of a human lung tissue ex vivo was conducted with the OFDI system. FIG. 19 depicts two images, A and B, obtained under identical experimental conditions except that  $\Delta f = 0$  for A and  $\Delta f = -2.5$  MHz for B. Each image was obtained using the mapping technique described above. The surface of the tissue was placed with an angle with respect to the probe beam axis, and the reference mirror was positioned such that the signal was present at both positive and negative depths in the image. In A, the tissue image is contained within the effective ranging depth of 2.8 mm, i.e. the top half of the total depth

WO 2005/047813 PCT/US2004/029148 -49-

span. However, the relatively large variation in the sample location resulted in the imaging folding artifact. In contrast, in B the entire positive and negative depths could be displayed without ambiguity taking advantage of the ranging depth increased to 5.8 mm by the frequency shifting technique.

5

10

The foregoing merely illustrates the principles of the invention. Various modifications and alterations to the described embodiments will be apparent to those skilled in the art in view of the teachings herein. It will thus be appreciated that those skilled in the art will be able to devise numerous systems, arrangements and methods which, although not explicitly shown or described herein, embody the principles of the invention and are thus within the spirit and scope of the present invention.